

RESIDUE CHEMISTRY GUIDELINES, 860 SERIES

I. Introduction.

The Residue Chemistry Guidelines are intended to provide instructions on how to conduct experiments to answer two questions:

(1) What is the nature of the residue that occurs in commodities when a pesticide is used on crops and/or livestock, i.e., what is the total toxic residue? and;

(2) How much total toxic residue results in commodities as a result of application of the pesticide to crops and/or livestock?

The “what” question is answered by Guideline 860.1300, Nature of the Residue. The “how much” question is answered by the remainder of the Guidelines.

II. Changes to The Guidelines.

Of all of the Residue Chemistry Guidelines the most significant scientific modifications from the 1982 Subdivision O were made to 860.1000, Background; 860.1300, Nature of the Residue; 860.1340, Residue Analytical Method; 860.1380, Storage Stability; 860.1480, Meat, Milk, Poultry and Eggs; 860.1500, Crop Field Trials; 860.1520, Processed Food/Feed; 860.1850, Confined Rotational Crops; and 860.1900, Field Rotational Crops. Highlights of the major changes in these topics are given below:

Background includes a revised Table I (formerly Table II), the list of raw agricultural and processed commodities considered to be foods and feeds. This is the modification of the table published in June 1994. Further revisions are in progress as a result of comments received by the Agency.

The test method for plant and livestock metabolism studies has been expanded to explain in much greater detail the protocol for conducting these studies. The procedure for analyzing the data generated has also been revised.

A requirement has been added to the residue analytical method for testing by an independent laboratory to ensure the procedure is suitable for enforcement purposes.

The procedure for conducting storage stability studies has been altered to allow data on representative commodities suffice for a number of other RACS or processed foods/feeds. Considerably more detail has also been provided on how to conduct the study.

The test method for conducting livestock feeding studies has been expanded to explain the protocol in greater detail.

The crop field trial guideline has been revised to formalize the number and location of trials required for most crops. Procedures for obtaining crop group tolerances and tolerances with regional registrations as well as special local need uses have been modified and explained in detail.

The procedures for performing processing studies and analyzing the data obtained from these studies to determine whether significant concentration is observed (and whether food/feed additive tolerances or Section 701 maximum residue limits are indicated) have been modified extensively.

The test method for conducting confined and field rotational crop studies has been modified to reflect dietary matters instead of environmental considerations. The requirement to conduct the

field rotational crop studies now involves a tiered approach. Also, the way in which the data from either experiment are analyzed has been revised to address the need for the establishment of rotational crop tolerances.

III. Description of The Guidelines.

A brief overview of each of the Residue Chemistry guideline requirements follows.

Background

This guideline provides general information on various requirements in the rest of the 860 series. The Table which provides a listing of crops, raw agricultural commodities (RACS), processed commodities and feed items is given in this guideline.

Nature of the Residue

This guideline requires metabolism studies on three dissimilar crops (unless the pesticide is registered on only 1 or 2 crops), ruminants and poultry. These should reflect application of radiolabeled pesticide to the plants in the manner that the chemical is to be used for pest control. Livestock are to be dosed orally with 14-C labeled pesticide unless the chemical is to be applied dermally in which case dermal metabolism studies are needed. Exaggerated application rates are encouraged in order to assure that enough radioactivity is observed in the plant and livestock RACS for identification of a major percentage of the total radioactive residue. This information is then used to determine the total toxic residue (TTR) to be expected in commodities.

Analytical Methods

The analytical methods provide the tool for answering the “how much” question. A method which measures the TTR in commodities is required for obtaining residue data on plants and livestock as well as for enforcement purposes. The method must pass an independent lab validation and an Agency method validation before it is deemed suitable for enforcement purposes. The Registrant must also provide data which indicates whether the TTR is measured in the FDA multi-residue procedures (PAM I).

Storage Stability

This requirement provides information on the integrity of the residue trial or feeding or processing study samples between the time the samples are taken and analysis. That is, is the level and make up of the TTR in the sample the same after frozen storage as it was at harvest? Storage stability data should reflect the same time interval as the residue samples were stored. The Agency prefers concurrent storage stability studies using samples stored in the same freezer as the samples from the corresponding residue study. Residue samples that are stored properly for 30 days or less need not be supported by storage stability data unless there is reason to believe that the TTR is unstable for a shorter period of time.

Crop Field Trials

This guideline requirement provides data on the maximum amount of residue to be expected in plant RACS as a result of application of typical end-use products to a crop using the directions provided on the label. The pesticide should be applied at the maximum treatment rate and appropriate RACS should be harvested according to the minimum preharvest interval prescribed in the label directions. Depending on the distribution of the crop over the USA and the agricultural and dietary importance of the crop/RACS, different numbers of field trials are required in various regions of the country. The number of trials needed range from 1 to 20 depending on the crop.

Processed Food/Feed

Processing studies are required to determine whether residues concentrate in processed commodities of those RACS which the Agency has determined to be generally processed. Samples of treated RACS are processed and the level of residues in the resulting fractions are determined. If residues concentrate significantly in a processed commodity, Section 409 food or feed additive tolerances or Section 701 maximum residue levels (MRL's) are established.

Meat, Milk, Poultry and Eggs

This guideline requirement is performed to determine whether residues occur in meat, milk, poultry or eggs as a result of direct application to livestock or the ingestion of feed items containing residues of a pesticide by livestock. In feeding studies animals are dosed orally at 1, 3 and 10X the estimated theoretical maximum dietary burden for at least 28 days or until levels of residues plateau in milk and/or eggs. Animals are sacrificed within 24 hours of the last dose and the appropriate tissue, milk and egg samples are taken and analyzed for TTR. For direct treatments, the animals are usually treated at the 1X rate according to the label directions. If residues occur in any commodity, tolerances must be established.

Confined Rotational Crops

Confined rotational crop studies are required to determine whether pesticide residues of concern (TTR) may occur in rotational crops as a result of treatment of primary crops. Soil is treated at a 1X rate with the radiolabeled pesticide and after appropriate time intervals, the rotational crops (usually a root crop, a leafy vegetable and a grain crop) are planted and RACS are harvested at various stages of growth reflecting typical harvest. The samples are analyzed for total radioactive residue and if significant levels of radioactivity are observed at the desired plant back interval (maximum one year considered practical) the nature of the radioactivity is determined as in a metabolism study. If residues of concern are observed, then the requirement for Field Rotational Crop studies is triggered.

Field Rotational Crops

These studies are required only if residues of concern are observed in the Confined Rotational Crop study (vide supra). Two studies are to be conducted for each of three dissimilar crops, again usually a root crop, a leafy vegetable and a grain crop for a total of six studies. These studies are conducted in a similar manner as discussed in the confined study above, although the pesticide is not radiolabeled. If quantifiable residues of concern are observed in the RACS of these crops, then additional crop field trials and establishment of rotational crop tolerances are required.

IV. Source Material.

The 860 series Residue Chemistry guidelines were prepared from the source types listed in the following paragraphs (with individual reference documents listed under each type). The new series of guidelines represents a consolidation of guidance developed since the guidelines were originally published in 1982.

Subdivision O, Residue Chemistry Guidelines.

U.S. Environmental Protection Agency, Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry. EPA Report No. 540/9-82-023, October, 1982. (Available from National Technical Information Service, Springfield, VA)

Guidance Documents.

U.S. Environmental Protection Agency, Pesticide Reregistration Rejection Rate Analysis – Residue Chemistry; Follow-up Guidance for: Generating Storage Stability Data; Submission of Raw Data; Maximum Theoretical Concentration Factors; Flowchart Diagrams. EPA Report No. 737–R–9–001, February, 1993.

U.S. Environmental Protection Agency, Pesticide Reregistration Rejection Rate Analysis – Residue Chemistry; Follow-up Guidance for: Updated Livestock Feeds Tables; Aspirated Grain Fractions (Grain Dust); A Tolerance Perspective; Calculating Livestock Dietary Exposure; Number and Location of Domestic CropField Trials. EPA Report No. 737–K–94–001, June, 1994.

FIFRA Guidance for Reregistration.

U.S. Environmental Protection Agency, Pesticide Reregistration Rejection Rate Analysis – Residue Chemistry; EPA Report No. 738–R–92–001, June, 1992. U.S. Environmental Protection Agency, FIFRA Accelerated Reregistration – Phase 3 Technical Guidance. EPA Report No. 540/09–90–078. (Available from National Technical Information Service, Springfield, VA).

Pesticide Registration (PR) Notices.

U.S. Environmental Protection Agency, Pesticide Registration (PR) Notice 88–5, Tolerance Enforcement Methods – Independent Laboratory Confirmation by Petitioner, July 15, 1988.

U.S. Environmental Protection Agency, Pesticide Registration (PR) Notice 86–5, Standard Format for Data Submitted under The FIFRA and Certain Provisions of the Federal Food, Drug, and Cosmetic Act (FFDCA), May 3, 1986.

U.S. Environmental Protection Agency, Pesticide Registration (PR) Notice 93–2, Waiver of Crop Field Trial Data for Aerial Applications, February 11, 1993.

Standard Evaluation Procedures.

U.S. Environmental Protection Agency, Standard Evaluation Procedure (SEP), Qualitative Nature of the Residue: Plant Metabolism, EPA Report No. 540/09–88–102. (Available from National Technical Information Service, Springfield, VA).

U.S. Environmental Protection Agency, Standard Evaluation Procedure (SEP), Qualitative Nature of the Residue: Metabolism in Food Animals, EPA Report No. 540/09–89–061. (Available from National Technical Information Service, Springfield, VA).

Data Reporting Guidance Documents.

U.S. Environmental Protection Agency, Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry, Series 171–4; Addendum No. 2 on Data Reporting, Magnitude of the Residue: Crop Field Trials, EPA Report No. 540/09–86–151 (Available from National Technical Information Service, Springfield, VA).

U.S. Environmental Protection Agency, Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry, Series 171–4; Addendum No. 3 on Data Reporting, Nature of the Residue: Plants, EPA Report No. 540/09–87–199. (Available from National Technical Information Service, Springfield, VA).

U.S. Environmental Protection Agency, Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry, Series 171–4; Addendum No. 4 on Data Reporting, Magnitude of the Residue:

Processed Food/Feed Study, EPA Report No. 540/09-88-004. (Available from National Technical Information Service, Springfield, VA).

U.S. Environmental Protection Agency, Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry, Series 171-4, Addendum No. 5 on Data Reporting, Specialty Applications, EPA Report No. 540/09-88-008. (Available from National Technical Information Service, Springfield, VA).

U.S. Environmental Protection Agency, Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry, Series 171-4(A)(3); Addendum No. 7 on Data Reporting, Metabolism (Qualitative Nature of the Residue): Food Animals, EPA Report No. 540/09-89-009. (Available from National Technical Information Service, Springfield, VA).

U.S. Environmental Protection Agency, Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry, Series 171-4; Addendum No. 8 on Data Reporting Residues in Meat, Milk, Poultry, and Eggs: Livestock Feeding Studies, EPA Report No. 540/09-89-010. (Available from National Technical Information Service, Springfield, VA).

Federal Register Notices.

U.S. Environmental Protection Agency, Pesticide Tolerances: Partial Response to Petition to Modify EPA Policy, OPP-260055; FRL-4944-2, June 14, 1995.

U.S. Environmental Protection Agency, Pesticide Tolerances; Revision of Crop Groups, Federal Register Notice 60 FR 26625-26643, May 17, 1995.

U.S. Environmental Protection Agency, Federal Register Notice 52 FR 24414- 24441, dated June 30, 1987.